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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,615	04/06/2001	William C. Olson	64672/JPW/SHS/NS	5850

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EXAMINER	
STUCKER, JEFFREY J	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/828,615	OLSON ET AL.	
	Examiner	Art Unit	
	Jeffrey Stucker	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,25-30 and 32-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,25,26,28-30 and 32-49* is/are rejected.

7)☒ Claim(s) *27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *16 Feb 05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This Office Action is in response to the amendment filed 16 February 2005. Claim 24 is canceled. Claims 23, 25-30, and 32-49 are pending and rejected.

The rejection of claims 23, 24, 48, 28, 29, 30, 32, and 33 under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Allaway et al. (6,107,019) is withdrawn.

The rejection of claims 23, 24, 48, 28, 29, 30, 32, and 33 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Progenics Pharmaceuticals, Inc. (Progenics), WO 97/47319 is withdrawn.

The rejection of claims 23-30, 32-44, 48, and 49 under 35 U.S.C. 103(a) as obvious over Allaway et al. (6,107,019) or Progenics Pharmaceuticals, Inc. (Progenics), WO 97/47319 is withdrawn.

The rejection of claims 23, 24, 48, and 45-47 under 35 U.S.C. 103(a) as obvious over Allaway et al. (6,107,019) or Progenics Pharmaceuticals, Inc. (Progenics), WO 97/47319, each in view of Cruse et al. is withdrawn.

The following is a new ground of rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23, 25, 26, 28-30, and 32-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administering antibody PA14 to reduce HIV viral load when administered solely after viral steady state is reached, does not reasonably provide enablement for anti-CCR5 antibodies that reduce HIV viral load when administered solely after viral steady state is reached. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561,

27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

As applicant has argued in previous responses filed 8/25/03, 6/25/04, and 2/16/05, the art is uncertain as to the predictability of using antibodies to reduce HIV viral load when administered solely after viral steady state is reached. One would expect that an antibody that binds to CCR5 and inhibits

HIV binding to the receptor would do so at all times. However, the review of the art suggested by applicant indicates that this is not the case. For example, applicant directed the Examiner's attention to two prior art references: Gauduin et al. (1997) Nature Medicine 3: 1389-93 ("Gauduin") and Poignard et al. (1999) Immunity 10: 431-8 ("Poignard"). Gauduin and Poignard both disclose a potently neutralizing anti-HIV-1 antibody that potently protects against infection with HIV-1 if administered at the time of, or up to several (6-24) hours after, viral challenge. Poignard demonstrates, however, that the same antibody affords *little or no therapeutic benefit in subjects* in which the HIV-1 viral load had reached steady state levels prior to administration of the antibody. In particular, Poignard discloses the administration of, *inter alia*, the IgG1b12 antibody. According to the authors of the reference:

> Neutralizing antibodies can protect against challenge with HIV-1 *in vivo* if present at appropriate concentrations at the time of viral challenge, but any role in the control of established infection is unclear (see Summary, p.431).

The authors went on to state (at p. 434, col. 2) that:

> In order to study the impact of neutralizing Abs on an ongoing HIV-1 infection, we have administered potent neutralizing Abs to HIV-1 infected hu-PBL-SCID mice after the infection had been established for some days, in most cases when the viral load had reached steady-state levels. Our results show that passive administration of either a single neutralizing human mAb or of a cocktail of three

such Abs has minimal effect on the control of an ongoing HIV-1 infection in the hu-PBL-SCID mouse model.

Turning to the Gauduin reference, although the IgG1b12 antibody was found to block infection when administered after HIV-1 challenge, this effect was obtained only when the antibody was administered no more than several hours after viral exposure, i.e., significantly before viral steady state reached. In contrast, claim 23 recites that the HIV-1 viral load of the HIV-1 infected subject is reduced when the antibody is administered "solely after viral steady state is reached."

The Poignard and Gauduin references thus clearly support the contention that antibodies useful for prophylactic treatment when administered prior infection often do not protect against an established HIV-1 infection. Thus, based on the prior art teachings of Poignard and Gauduin, one skilled the art the time the invention was made could not have predicted and certainly would not have had an expectation that treatment administered solely after viral steady state had been reached would be efficacious. One of ordinary skill in the art, armed with the knowledge that an anti-HIV-1 antibody that completely protects against acute HIV-1 infection may be completely ineffective against chronic HIV-1 infection, could not have predicted and would have had no reasonable expectation of success that an

anti-CCR5 antibody would prove efficacious in reducing the viral load in chronically HIV-1-infected subjects with steady state HIV-I levels.

Though the antibody of Poignard and Gauduin is directed to an epitope of HIV-1 gp120 whereas the antibodies recited in the instant claims are directed to an epitope of the CCR5 chemokine receptor, the identity of the antibodies is secondary to the general principle taught by the prior art references. Indeed, Poignard's results on the effect of HIV-1 neutralizing antibodies in subjects with steady state HIV-1 levels are not limited to a particular antibody. Instead, these results "show that passive administration of either a single neutralizing human mAb or of a cocktail of three such Abs has minimal effect on the control of an ongoing HIV-1 infection in the hu-PBL-SCID mouse model" (page 434, first paragraph of the "Discussion" in Poignard). Thus, the more salient principle taught by Gauduin and Poignard is clearly that the prophylactic efficacy of an anti-HIV-1 antibody in protecting against acute HIV-I infection is not predictive of therapeutic efficacy against a chronic HIV-1 infection, characterized by steady state viral levels, as claimed in the subject invention.

The above uncertainty is not remedied by applicant's specification which is lacking in working examples. The only

working example is found on pages 96 and 97 which is directed solely to testing the efficacy of monoclonal antibody PA14. This example provides support for the claims limited to this particular antibody. However, given the uncertainty of the art in regards to treatment with antibodies after viral steady state has been reached, this does not provide support for the full scope of the claims.

The instant invention, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

Claim 27 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claims are allowed.

Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

The Group 1600 Official Fax number is: (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval

(PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Stucker whose telephone number is (571)-272-0911. The examiner can normally be reached Monday to Thursday from 7:00am-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (571)-272-0902.

JEFFREY STUCKER
PRIMARY EXAMINER